We Claim

1. A method of amplification of a nucleic acid sample comprising:

(a) obtaining a nucleic acid sample;

(b) contacting the nucleic acid sample with the appropriate reagents to synthesize a first strand cDNA;

(c) synthesizing a second strand cDNA in a reaction mixture comprising dUTP;

(d) nicking the second strand cDNA at one or more positions where dUTP was incorporated to generate one or more nicks; and

(e) extending the second strand cDNA from the one or more nicks in a reaction mixture comprising dUTP and a DNA polymerase with strand displacing activity, wherein downstream fragments of the second strand cDNA are displaced.

2. The method of claim 1 wherein steps (d) and (e) are performed simultaneously in a single reaction.

3. The method of claim 1 wherein step (d) comprises: generating abasic sites in the second strand cDNA and cleaving the second strand cDNA at the abasic sites.

4. The method of claim 3 wherein the abasic sites are generated by incubating with a uracil DNA glycosylase enzyme.

5. The method of claim 3 wherein the step of cleaving the second strand cDNA at the abasic sites comprises incubating the second strand cDNA with an apurinic endonuclease.

6. The method of claim 5 wherein the apurinic endonuclease is Endonuclease IV

7. The method of claim 3 wherein the step of cleaving the second strand cDNA at abasic sites comprises incubating the second strand cDNA at high temperature.

8. The method of claim 3 wherein the step of cleaving the second strand cDNA at abasic sites comprises incubating the second strand cDNA under alkaline conditions.

9. The method of claim 1 wherein first strand cDNA is synthesized in the presence of an RNA dependent DNA polymerase and second strand cDNA is synthesized in the presence of a DNA dependent DNA polymerase.

10. The method of claim 1 wherein the strand displacing DNA polymerase is selected from the group consisting of the Klenow fragment, Bst and phi29.

11. The method of claim 1 wherein the DNA polymerase is a phi29 variant that has reduced exonuclease activity.

12. The method of claim 1 wherein steps (d) and (e) are performed under isothermal conditions.

13. The method of claim 1 wherein steps (d) and (e) are performed at 37°C.

14. The method of claim 1 wherein Endonuclease V is used to nick the second strand cDNA in step (d).

15. The method of claim 1 wherein the reaction mixture of step (c) further comprises dTTP and the ratio of dTTP to dUTP in the starting mixture is greater than about 5 to 1.

16. The method of claim 1 the reaction mixture of step (e) further comprises a labeled nucleotide.

17. The method of claim 16 wherein the labeled nucleotide is biotin-dATP.

18. The method of claim 1 wherein the first strand cDNA is synthesized by a method comprising: hybridizing at least one primer to the nucleic acid sample and extending the primer with a polymerase.

19. The method of claim 18 wherein the nucleic acid sample comprises RNA and the polymerase is an RNA dependent DNA polymerase.

20. The method of claim 18 wherein the at least one primer comprises a 3' oligo dT portion.

21. The method of claim 18 wherein the at least one primer comprises a mixture of primers of random sequence wherein the primers are of a common length and the length is between 6 and 15 nucleotides.

22. A method of detecting a target sequence in a nucleic acid sample comprising a complex mixture of sequences comprising:

(a) amplifying the nucleic acid sample by the method of claim 1;

(b) labeling the nucleic acids in the amplified nucleic acid sample with a detectable label;

(c) hybridizing the labeled, amplified nucleic acids to an array of probes comprising at least one probe that is perfectly complementary to the target sequence over the length of the probe;

(d) detecting a hybridization pattern; and,

(e) determining if the target sequence is present or absent based on the hybridization pattern.

23. The method of claim 21 wherein the label is biotin.

24. The method of claim 1 wherein the nucleic acid sample comprises RNA and first strand cDNA is synthesized using an RNA dependent DNA polymerase.

25. The method of claim 20 wherein first strand cDNA is synthesized by a primer comprising oligo dT.

26. The method of claim 20 wherein first strand cDNA synthesis is primed by a plurality of locus specific primers.

27. The method of claim 1 wherein the nucleic acid comprises genomic DNA.

28. The method of claim 23 wherein first strand cDNA synthesis is primed by a plurality of locus specific primers.

29. The method of claim 1 wherein the nucleic acid sample comprises adaptor ligated DNA fragments.

30. The method of claim 1 wherein the nucleic acid sample comprises adaptor ligated DNA fragments that have been amplified by PCR.

31. A method of genotyping at least one polymorphism from a sample comprising:

(a) obtaining a nucleic acid sample;

(b) contacting the nucleic acid sample with the appropriate reagents to synthesize a first strand cDNA from the nucleic acid sample;

(c) synthesizing a second strand cDNA in a reaction mixture comprising dUTP;

(d) nicking the second strand cDNA at one or more positions where dUTP was incorporated to generate one or more nicks in the second strand cDNA; and

(e) extending the second strand cDNA from the one or more nicks in a reaction mixture comprising dUTP and a DNA polymerase with strand displacing activity, wherein downstream fragments of the second strand cDNA are displaced by the DNA polymerase to generate displaced fragments;

(f) labeling the displaced fragments with a detectable label;

(g) hybridizing the labeled displaced fragments to an array of probes comprising at least one probe that is perfectly complementary to the target sequence over the length of the probe;

(a) detecting a hybridization pattern; and,

(b) determining if the target sequence is present or absent based on the hybridization pattern.

32. The method of claim 31 wherein the array of probes comprises a plurality of genotyping probe sets wherein each probe set comprises a first probe that is perfectly complementary to a first allele of a SNP and a second probe that is perfectly complementary to a second allele of the SNP wherein the first and second probes are between 20 and 50 nucleotides in length and the central position of each probes is complementary to the polymorphic position of the SNP.

33. A kit for amplifying nucleic acids comprising: a strand displacing DNA polymerase, dUTP, and uracil DNA glycosylase.

34. The kit of claim 33 further comprising Endonuclease IV.

35. The kit of claim 33 further comprising an RNA dependent DNA polymerase and a primer.

36. A kit for amplifying nucleic acids comprising: a strand displacing DNA polymerase, dUTP, and Endonuclease V.

37. The kit of claim 36 further comprising an RNA dependent DNA polymerase and a primer.